

WHAT IS CLAIMED IS:

1 ~~Sub~~ 1. A non-toxic *Pseudomonas* exotoxin A-like ("PE-like") chimeric
2 immunogen comprising: (1) a cell recognition domain of between 10 and 1500 amino
3 acids that binds to a cell surface receptor; (2) a translocation domain comprising an
4 amino acid sequence substantially identical to a sequence of PE domain II sufficient to
5 effect translocation to a cell cytosol; (3) a non-native epitope domain comprising an
6 amino acid sequence of between 5 and 1500 amino acids that encodes a non-native
7 epitope; and (4) an amino acid sequence encoding an endoplasmic reticulum ("ER")
8 retention domain that comprises an ER retention sequence.

1 2. The immunogen of claim 1 having the amino acid sequence of PE
2 Δ E553 except that the sequence of domain Ib of PE Δ E553 comprises the non-native
3 epitope between two cysteine residues of domain Ib.

1 3. The immunogen of claim 1 wherein the cell recognition domain is
2 domain Ia of PE.

1 4. The immunogen of claim 1 wherein cell recognition domain binds
2 to α 2-macroglobulin receptor (" α 2-MR"), epidermal growth factor ("EGF") receptor; the
3 IL-2 receptor; the IL-6 receptor; HIV-infected cells; a chemokine receptor; a leukocyte
4 cell surface receptor; a ligand for the IgA receptor; or an antibody or antibody fragment
5 directed to a receptor.

1 5. The immunogen of claim 1 wherein cell recognition domain
2 comprises amino acid sequences of a growth factor or an antibody.

1 6. The immunogen of claim 1 wherein cell recognition domain is
2 comprised within the ER retention domain.

1 ~~Sub~~ 7. The immunogen of claim 1 wherein the translocation domain
2 comprises amino acids 280 to 364 of domain II of PE.

1 8. The immunogen of claim 1 wherein the translocation domain is
2 domain II of PE.

1 9. The immunogen of claim 1 wherein the ~~non-native epitope~~ domain
2 comprises a cysteine-cysteine loop that comprises the non-native epitope.

1 10. The immunogen of claim 1 wherein the non-native epitope domain
2 comprises an amino acid sequence encoding a non-native epitope inserted between two
3 cysteine residues of domain Ib of PE.

1 11. The immunogen of claim 1 wherein the non-native epitope domain
2 comprises an amino acid sequence selected from CTRPNYNKRK RIHIGPGRAF
3 YTTKNIIGTI RQAHC (SEQ ID NO:3) or CTRPSNTRT SITIGPGQVF YRTGDIIGDI
4 RKAYC (SEQ ID NO:4).

1 12. The immunogen of claim 1 wherein the ER retention domain is
2 domain III of PE comprising the mutation Δ E553.

1 13. The immunogen of claim 1 wherein the ER retention sequence
2 comprises REDLK (SEQ ID NO:11), REDL (SEQ ID NO:12) or KDEL (SEQ ID
3 NO:13).

1 14. The immunogen of claim 1 which is ntPE-V3MN14 or ntPE-
2 V3MN26.

1 15. The immunogen of claim 1 wherein the non-native epitope is an
2 epitope from a viral, bacterial or parasitic protozoan pathogen.

1 16. The immunogen of claim 9 wherein the non-native epitope is an
2 epitope of a V3 loop of gp120 of HIV-1.

1 17. The immunogen of claim 9 wherein the non-native epitope is an
2 epitope of a principal neutralizing loop of a retrovirus.

1 18. The immunogen of claim 9 wherein the non-native epitope is an
2 epitope of a major neutralizing loop of HIV-2 or a V3 loop of gp120 of HIV-1 of at least
3 8 amino acids including a V3 loop apex.

1 19. A recombinant polynucleotide comprising a nucleotide sequence
2 encoding a non-toxic *Pseudomonas* exotoxin A-like ("PE-like") chimeric immunogen, the
3 PE-like chimeric immunogen comprising: (1) a cell recognition domain of between 10
4 and 1500 amino acids that binds to a cell surface receptor; (2) a translocation domain
5 comprising an amino acid sequence substantially identical to a sequence of PE domain II
6 sufficient to effect translocation to a cell cytosol; (3) a non-native epitope domain
7 comprising an amino acid sequence of between 5 and 1500 amino acids that encodes a
8 non-native epitope; and (4) an amino acid sequence encoding an endoplasmic reticulum
9 ("ER") retention domain that comprises an ER retention sequence.

1 20. The recombinant polynucleotide of claim 19 which is an expression
2 vector further comprising an expression control sequence operatively linked to the
3 nucleotide sequence.

1 21. The recombinant polynucleotide of claim 19 having the amino acid
2 sequence of PE wherein domain Ib of PE further comprises the non-native epitope
3 between two cysteine residues of domain Ib.

1 22. A recombinant non-toxic *Pseudomonas* exotoxin A-like ("PE-like")
2 chimeric immunogen cloning platform comprising a nucleotide sequence encoding: (1) a
3 cell recognition domain of between 10 and 1500 amino acids that binds to a cell surface
4 receptor; (2) a translocation domain comprising an amino acid sequence substantially
5 identical to a sequence of PE domain II sufficient to effect translocation to a cell cytosol;
6 (3) an amino acid sequence encoding an endoplasmic reticulum ("ER") retention domain
7 that comprises an ER retention sequence and (4) a splicing site between the sequence
8 encoding the translocation domain and the sequence encoding the ER retention domain.

1 23. The recombinant cloning platform of claim 22 which is an
2 expression vector further comprising an expression control sequence operatively linked to
3 the nucleotide sequence.

1 24. A method of producing antibodies against a non-native epitope,
2 wherein the non-native epitope naturally exists within a cysteine-cysteine loop comprising
3 the step of inoculating an animal with a non-toxic *Pseudomonas* exotoxin A-like ("PE-
4 like") chimeric immunogen, the PE-like chimeric immunogen comprising: (1) a cell
5 recognition domain of between 10 and 1500 amino acids that binds to a cell surface
6 receptor; (2) a translocation domain comprising an amino acid sequence substantially
7 identical to a sequence of PE domain II sufficient to effect translocation to a cell cytosol;
8 (3) a non-native epitope domain comprising a cysteine-cysteine loop that contains within
9 the loop an amino acid sequence of between 5 and 1500 amino acids that encodes a non-
10 native epitope; and (4) an amino acid sequence encoding an endoplasmic reticulum
11 ("ER") retention domain that comprises an ER retention sequence.

1 25. The method of claim 24 wherein the cysteine-cysteine loop
2 comprises no more than about 30 amino acids.

1 26. The method of claim 24 wherein the non-native epitope is an
2 epitope of the V3 domain of HIV-1.

1 27. A vaccine comprising at least one non-toxic *Pseudomonas* exotoxin
2 A-like ("PE-like") chimeric immunogen, the PE-like chimeric immunogen comprising:
3 (1) a cell recognition domain of between 10 and 1500 amino acids that binds to a cell
4 surface receptor; (2) a translocation domain comprising an amino acid sequence
5 substantially identical to a sequence of PE domain II sufficient to effect translocation to a
6 cell cytosol; (3) a non-native epitope domain comprising an amino acid sequence of
7 between 5 and 1500 amino acids that encodes a non-native epitope; and (4) an amino
8 acid sequence encoding an endoplasmic reticulum ("ER") retention domain that
9 comprises an ER retention sequence.

1 28. The vaccine of claim 27 comprising a plurality of PE-like chimeric
2 immunogens, each immunogen having a different non-native epitope.

1 29. The vaccine of claim 27 further comprising a pharmaceutically
2 acceptable carrier.

1 30. The vaccine of claim 27 in the form of an immunization dose
2 wherein the immunogen is present in an amount effective to elicit in a human subject an
3 immune response against the non-native epitope.

1 31. The vaccine of claim 28 wherein the different non-native epitopes
2 are epitopes of different strains of the same pathogen.

1 32. The vaccine of claim 31 wherein the non-native epitope is an
2 epitope of the V3 loop of HIV-1 and the different strains of the same pathogen are HIV-1
3 MN and HIV-1 Thai-E.

1 33. A method of eliciting an immune response against a non-native
2 epitope in a subject, the method comprising the step of administering to the subject a
3 vaccine comprising at least one non-toxic *Pseudomonas* exotoxin A-like ("PE-like")
4 chimeric immunogen, the PE-like chimeric immunogen comprising: (1) a cell recognition
5 domain of between 10 and 1500 amino acids that binds to a cell surface receptor; (2) a
6 translocation domain comprising an amino acid sequence substantially identical to a
7 sequence of PE domain II sufficient to effect translocation to a cell cytosol; (3) a non-
8 native epitope domain comprising an amino acid sequence of between 5 and 1500 amino
9 acids that encodes a non-native epitope; and (4) an amino acid sequence encoding an
10 endoplasmic reticulum ("ER") retention domain that comprises an ER retention sequence.

1 34. The method of claim 33 wherein the non-native epitope comprises a
2 binding motif for an MHC Class II molecule of the subject and the immune response
3 elicited is an MHC Class-II dependent cell-mediated immune response.

1 35. The method of claim 33 wherein the non-native epitope comprises a
2 binding motif for an MHC Class I molecule of the subject and the immune response
3 elicited is an MHC Class-I dependent cell-mediated immune response.

1 36. The method of claim 33 wherein the non-native epitope is an
2 epitope of the V3 domain of HIV-1.

1 37. The method of claim 33 wherein the vaccine is administered as a
2 prophylactic treatment against a disease mediated by an agent bearing the non-native
3 epitope.

1 38. The method of claim 33 wherein the vaccine is administered as a
2 therapeutic treatment against a disease mediated by an agent bearing the non-native
3 epitope.

1 39. A polynucleotide vaccine comprising at least one recombinant
2 polynucleotide comprising a nucleotide sequence encoding a non-toxic *Pseudomonas*
3 exotoxin A-like ("PE-like") chimeric immunogen, the PE-like chimeric immunogen
4 comprising: (1) a cell recognition domain of between 10 and 1500 amino acids that binds
5 to a cell surface receptor; (2) a translocation domain comprising an amino acid sequence
6 substantially identical to a sequence of PE domain II sufficient to effect translocation to a
7 cell cytosol; (3) a non-native epitope domain comprising an amino acid sequence of
8 between 5 and 1500 amino acids that encodes a non-native epitope; and (4) an amino
9 acid sequence encoding an endoplasmic reticulum ("ER") retention domain that
10 comprises an ER retention sequence.

1 40. A method of eliciting an immune response against a non-native
2 epitope in a subject, the method comprising the step of administering to the subject a
3 polynucleotide vaccine comprising at least one recombinant polynucleotide comprising a
4 nucleotide sequence encoding a non-toxic *Pseudomonas* exotoxin A-like ("PE-like")
5 chimeric immunogen, the PE-like chimeric immunogen comprising: (1) a cell recognition
6 domain of between 10 and 1500 amino acids that binds to a cell surface receptor; (2) a
7 translocation domain comprising an amino acid sequence substantially identical to a

8 sequence of PE domain II sufficient to effect translocation to a cell cytosol; (3) a non-
9 native epitope domain comprising an amino acid sequence of between 5 and 1500 amino
10 acids that encodes a non-native epitope; and (4) an amino acid sequence encoding an
11 endoplasmic reticulum ("ER") retention domain that comprises an ER retention sequence.

1 41. The method of claim 40 wherein the recombinant polynucleotide is
2 an expression vector comprising an expression control sequence operatively linked to the
3 nucleotide sequence.

1 42. The method of claim 40 wherein the nucleotide sequence further
2 encodes a mammalian secretory sequence attached to the amino terminus of the
3 immunogen.

1 43. A method of eliciting an immune response against a non-native
2 epitope in a subject, the method comprising the steps of transfecting cells with a
3 recombinant polynucleotide comprising a nucleotide sequence encoding a non-toxic
4 *Pseudomonas* exotoxin A-like ("PE-like") chimeric immunogen, the PE-like chimeric
5 immunogen comprising: (1) a cell recognition domain of between 10 and 1500 amino
6 acids that binds to a cell surface receptor; (2) a translocation domain comprising an
7 amino acid sequence substantially identical to a sequence of PE domain II sufficient to
8 effect translocation to a cell cytosol; (3) a non-native epitope domain comprising an
9 amino acid sequence of between 5 and 1500 amino acids that encodes a non-native
10 epitope; and (4) an amino acid sequence encoding an endoplasmic reticulum ("ER")
11 retention domain that comprises an ER retention sequence, and administering the cells to
12 the subject.

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